REMARKS

Following entry of the present Response and Amendment, claims 1-11, and 13-24, and 26-32 remain pending in this application, with claim 1 being the only independent claim.

The Office Action dated January 25, 2010 (the "Office Action") rejected all claims based under 35 U.S.C. § 103 as allegedly being rendered obvious by various combinations of the following references, among others: U.S. Patent Application Pub. No. 2003/0087877 (henceforth, "'877 Publication"), a 1995 article "Water-soluble ..." by Klein, U.S. Patent Application Pub. No. 2002/0037874 (henceforth, "'874 Publication"), and U.S. Patent No. 6,335,029 (henceforth, "'029 Patent").

In the present Response and Amendment, independent claim 1 has been amended herein to include the features of original claim 25. Claim 12 has thus been cancelled. Claim 1 has also been amended herein to more accurately reflect the scope embodied by the language of original claim 12 (claim 1 having been previously amended to include the limitations of claim 12). Various dependent claims have been amended to correct dependency, antecedent basis, and typographical inconsistencies, including claims 15, 17, 26, 32, and 42. Claims 1-11, 13-24, 26-32, and 42 thus remain pending in the application.

Applicant respectfully requests reconsideration of the merits of the present application in accordance with these amendments and the following remarks.

35 U.S.C. § 103 Rejections

Independent claim 1 as presently amended incorporates the limitations of original dependent claims 12 and 25. The Office Action based its obviousness rejection of the subject matter of previously pending independent claim 1 and original dependent claim 25 upon a combination of the '877 Publication, in view of Klein, the '874 Publication, and the '029 Patent. Insofar as this rejection applies to the claims as presently amended, Applicant respectfully traverses as follows.

Applicant's lone independent claim recites a method for preparing a drug eluting medical device that includes three steps. In sum, the steps include: applying a drug to the device, thereafter applying a polymer to the device, and then depositing biological molecules on the surface of the polymer. The method is further limited in that the step of applying the polymer is done via cold plasma and in a single step, and in that the polymer has active

functional groups capable of chemically binding biological molecules.

The '029 Patent discloses an implantable medical device comprising at least one layer (5) comprised of at least one bioactive agent in a polymeric matrix, and at least one barrier (20) positioned over the layer. The barrier may incorporate a bioactive agent, and the barrier layer (20) is formed in situ by a low energy plasma polymerization process of a monomer gas or by a vapour deposition process. This barrier (20) is taught as being for the purpose of controlling the release of the bioactive agent. *See, e.g.*, '029 Patent at column 7, lines 33-34. Nothing in this reference teaches or suggest that the outer barrier layer could or should contain any active functional groups for chemically binding the bioactive agent compounds being deposited over a layer containing a bioactive agent. While the '029 discloses that the barrier layer of its device may be dipped or sprayed in heparin, this disclosure **would not** be understood by one skilled in the art as meaning that the barrier layer has (or should have) any type of functional groups for chemically binding the heparin. Further, the '029 Patent is absent any disclosure, teaching, or suggestion that a barrier layer having such functional groups should or could be produced in a single-step process by means of cold plasma application. The '029 Patent is clearly lacking any teaching or suggestion regarding (1) the use of chemical binding groups in the barrier layer to bind the bioactive agent, and (2) the formation of a barrier layer by using cold plasma to form a polymer layer having active functional groups capable of binding the bioactive agent. Claim 1 is thus distinguishable over the base reference '029 Patent for at least these reasons.

KSR addressed the situation where multiple references are combined to render an invention obvious by noting that a "combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." See *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 82 USPQ2d 1385 (2007). KSR, however, should not be seen as a making any combination of references suitable for a proper obviousness rejection so long as every element of the claimed invention is present in at least one of the multitude of references First, "rejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.'" *KSR*, 82 USPQ2d at 1396, quoting *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006). See also MPEP 2143.01. Second, while obviousness does not require absolute predictability when

combining references, a degree of predictability is required. See MPEP 2143.01. In this regard, a showing by the Applicant that one skilled in the art in fact would **not** find a reasonable expectation of success in the Examiner's asserted combination supports a conclusion of nonobviousness. See *In re Rinehart*, 531 F.2d 1048, 189 USPQ 143 (CCPA 1976), and MPEP 2143.01.

The Office Action attempts to remedy the deficiencies of the '029 Patent by relying principally upon the '877 Publication and Klein. Applicant has made several arguments previously upon the record attacking the combination of these references with the '029 Patent by noting that one skilled in the art would not find a reasonable expectation of success in combining these references. However, the Office Action wholly ignores those arguments, and instead improperly concludes that Applicant is merely attacking the references individually. This is completely untrue. Applicants prior and current remarks not only point out the differences between each asserted reference and the claimed invention, but also explains how differences between the asserted references make them an illogical combination in the view of one skilled in the art. Applicant has explained previously on the record, and summarizes the reasoning again below, that the prior art references of record cannot be properly combined with any reasonable expectation of success to teach all limitations of claim 1.

In the obviousness rejection, the Office Action alleges that the '877 Publication and Klein can be read together as teaching on skilled in the art use cold plasma deposition of a polymer containing amino groups to bind a biological molecule, such as heparin, in a "single step" as recited in claim 1. In making this conclusion, the Office Action completely disregards the teachings of the '877 Publication that the polymer must be **surface treated** with a Traut's reagent after the cold plasma deposition, and then application of an activating agent. The Office Action disputes this argument of Applicant by countering, incorrectly that "the '877 Publication does not specifically teach that a biomeolecule could no be reacted with the free amino bonds of the plasma treated surface." This is untrue. The'877 Publication explicitly teaches at paragraphs 14-17 that the binding of the polymer and biomolecules are achieved through a disulfide bond. This disulfide bond is created by cleavage of the disulfide bond of the polymer with a reactive thiol group found on the therapeutic agent (par. 17), or by the formation of active thiol groups on the polymer substrate (par. 25). In cases where the

therapeutic agent does not have a thiol group, the therapeutic agent is modified chemically (par. 14), such as by a reaction with Traut's Reagent (par. 22), to have a thiol group while the therapeutic agent is modified to have a disulfide linkage (par. 25). Nowhere does the '877 Publication disclose the attachment of therapeutic agents via an amino group to an untreated polymer substrate, as alleged by the Office Action, but rather that either the substrate or therapeutic agent must be modified. Thus, in all aspects of the invention disclosed in the '877 Publication, the polymer surface created by cold plasma **does not** have "active functional groups capable of chemically binding biological molecules." Instead, the surface **must** be treated in at least one additional step to create the thiol groups.

Therefore, the '877 Publication does not teach or suggest creating via cold plasma in a single step "a polymer active functional groups capable of chemically binding biological molecules." These extra steps are taught as being necessary by the '877 Publication, and cannot be ignored by the Examiner by simply arguing without support that one skilled in the art would be motivated to reduce unnecessary steps. The entirety of the '877 Publication teaches that these steps extra steps following cold plasma formation of the polymer are essential, and the Examiner has provided no reasonable explanation why one skilled in the art would conclude that a single step process would be achieved contrary to this essential step.

In relying upon Klein, the Office Action appears to argue that one skilled in the art would be motivated to deposit a polymer having active functional groups capable of chemically binding biological molecules onto a medical device by cold plasma because Klein allegedly teaches the reaction of heparin with a poly(acrylamide-allylamine) derivative. Even if Klein teaches as alleged, this still does not provide one skilled in the art with the motivation to produce applicant's claimed invention. Nothing in Klein would suggest to skilled in the art to modify the process of the '877 Publication. It does not relate in any way to cold plasma deposition of polymers, or creating drug eluting stents, or even to creating biocompatible medical implants. Thus, again, one skilled in the art would have no reasonable expectation of success, and therefore would not be motivated to eliminate what are taught as being essential steps by the '877 Publication. The Examiner's combination of references therefore solely a hindsight recreation using Applicant's specification as a guide.

Not only is the Examiner employing impermissible hindsight, but she is ignoring the fact that, one skilled in the art would not have been able to predict the behavior of a plasma-

deposited allylamine polymer of the '877 Publication if reacted in the same manner as the polyacrylamide of Klein. First, the polyacrylamide has amide groups, whereas the allylamine plasma deposited conserves amino groups, which do react very differently. Second, the polyacrylamide is very hydrophilic and tends to hydrate, while plasma deposited allylamine is hydrophobic, as also disclosed in the present application. See, application at par. 20. In fact, the fact that the plasma deposited polymer is hydrophobic makes it particularly suitable as a means for treating drug eluting stents, as it prevents the stent from losing the drug during subsequent treatment to add the biocompatible anti-thrombogenic outer layer.

Thus, polyacrylamide could not have been taken as a close equivalent of the plasma deposited allylamine and one skilled in the art would not be motivated to make the leap of logic posited by the Office Action.

Finally, the '874 Publication likewise fails to remedy these deficiencies of the '877 Publication and '029 Patent. The '874 Publication teaches only sulphated derivatives of hyaluronic acid that can be useful for their anti-thrombogenic properties. Again, nothing in that reference would lead one skilled in the art to deposit by cold plasma a polymer having active functional groups capable of chemically binding biological molecules.

Claim 1 as presently amended further distinguishes over the prior art because it recites depositing biological molecules on the surface of the polymer where the biological molecules have stable reactive functional groups (from claim 25). In rejecting previously presented dependent claim 25, the Office Action made the assertion that alleges that the '877 Publication teaches this feature. This, again, is untrue. The cited portion of the '877 Publication (par. 52), describes the use of Traut's Reagent and HA-NEA to prepare the surface of the polymer and create thiols on the surface of the polymer. Again, one skilled in the art, as noted above, would see no reason to modify the multi-step process disclosed in the '877 Publication to remove these essential steps, and neither Klein nor the '874 Publication provide any motivation to do so. In making the present obviousness rejection of claim 1, the Office Action therefore is applying an improper hindsight analysis and ignoring the fact that one skilled in the art would see no reasonable expectation of success to modify the references as indicated.

As such, the Examiner cannot modify the '877 Publication to her liking by simply ignoring portions of the reference that are inconvenient. The '877 Publication does not

disclose forming a polymer layer having active functional groups capable of binding in a single step via cold plasma means. There would be reasonable expectation of success in removing the essential steps taught in the '877 Publication, and the Klein reference provides no remedy to these deficiencies. As such, the entire combination of references fails, making the Examiner's entire *prima facie* case for obviousness improper.

Finally, Applicant notes that the various other prior art references cited in the Office Action against various other dependent claims do not contain any of the features described above as distinguishing claim 1 from the prior art. As such, since claim 1 is the sole independent claim pending in this application, all claims are allowable over the prior art of record for the reasons set forth herein.

Favorable consideration of the above remarks and claims, and a timely Notice of Allowance is thus respectfully requested.

Conclusion

In view of the foregoing, the Applicant respectfully requests that the Examiner enter the above-noted amendments, and that the above remarks be fully considered in conjunction reconsidering the present claims. Timely allowance of all pending claims and the issuance of a Notice of Allowance are requested.

While none are believed to be necessary at this time, if additional claims fees are believed due at this time in connection with this Response and Amendment, or if the appropriate fees have not been paid for the one-month extension of time requested herewith, please charge the fees to our Deposit Account No. 50-1349. Also, please credit any previous overpayments to Deposit Account No. 50-1349.

The Examiner is invited to contact Applicant's undersigned representative via telephone to discuss the present Response and Amendment if any issues are found in the present claims. Applicant believes such a telephone call would likely progress prosecution of this application toward allowance more quickly than would mailing of a further Office Action.

Respectfully submitted,

Dated: April 26, 2010

By: _____
Kevin G. Shaw
Registration No. 43,110

HOGAN & HARTSON LLP
555 13th Street, N.W.
Washington, D.C. 20004
Telephone: 202-637-5600
Facsimile: 202-637-5910
email: dcpatents@hhlaw.com
Customer No.: 24933